



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/571,285

03/09/2006

Kenji Hayashi

1056-0134PUS1

8225

2292 7590 04/15/2009
BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER

BIANCHI, KRISTIN A

ART UNIT

PAPER NUMBER

1626

NOTIFICATION DATE

DELIVERY MODE

04/15/2009

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No. 10/571,285	Applicant(s) HAYASHI ET AL.	
	Examiner KRISTIN BIANCHI	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>01/09/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-3 are pending in the instant application. Claims 1-3 are rejected.

Information Disclosure Statement

The information disclosure statement filed on January 9, 2009 has been considered and a signed copy of form 1449 is enclosed herewith. It is noted that the references (i.e., WO 00/50395 A1, WO 02/36117 A1 and WO 02/059092 A1) which were stricken out or not considered on the IDS filed on March 9, 2006 have now been considered.

Priority

It is noted that a copy of the JP 2003-318974 priority document has been received from the International Bureau of WIPO.

Response to Arguments/Remarks

The remarks filed on January 9, 2009 have been fully considered. In regards to the 35 U.S.C. 103(a) rejection of claims 1-3, Applicants' argue that both Owa et al. and Haneda et al. never teach or suggest that the reactions can be carried out in a mixed solvent of water and C1-6 alkyl acetate. This has not found to be persuasive because as mentioned in the office action dated September 12, 2008, "it is common practice for a person skilled in the art to carry out a synthesis in different solvent conditions in an attempt to optimize a synthesis." Also, Applicants disclose in their remarks that in Haneda et al. (paragraph [0020]) it is disclosed that "although there is no particular limitation for the solvent used for the reaction, those which dissolve the material substances and do not readily react with them are preferred." Owa et al. uses ethyl

Art Unit: 1626

acetate as a solvent in the reaction and it is also disclosed in paragraph [0020] of Haneda et al. that a mixed solvent can be used. One of ordinary skill in the art would have known that a mixture of C1-6 alkyl acetate and water could dissolve the material substances and would not readily react with them (i.e., could be a useful solvent in the reaction). Therefore, it would have been obvious to one of ordinary skill to experiment with different solvents and/or mixtures of solvents in an attempt to find the optimal reaction conditions and to arrive at the mixed solvent which is used in the instant invention. One of skill would also be motivated to carry out the reaction disclosed in Haneda et al. with a different solvent than the one disclosed in the examples (i.e., THF in the presence of pyridine) because it was known in the art at the time of the invention that THF tends to form peroxides as mentioned in the office action dated September 12, 2008. Applicants' also argue that it is not true that the one-pot process disclosed in Crassier et al. gives better yields compared to the stepwise synthesis. This argument has not been found to be persuasive because even if the yield of the one-pot synthesis disclosed in Crassier et al. is remarkably lower than that by stepwise synthesis according to the Applicants' calculations, Crassier et al. is still suggesting that a one-pot process gives better yields (i.e., page 7, lines 7 and 8). Therefore, it is not believed by the examiner that Crassier et al. teaches away from the one-pot process and the suggestion mentioned above would motivate one of skill in the art to attempt the one-pot process and to arrive at the instant invention. Therefore, Applicants' arguments have not been persuasive and the 35 U.S.C. 103(a) rejection of claims 1-3 is maintained.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

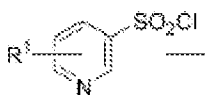
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haneda et al. (US 2002/0128480) in view of Owa et al. (Bioorganic and Medicinal Chemistry Letters 12 (2002) 2097-2100) and Crassier et al. (WO 02/059092) further in view of <http://en.wikipedia.org/wiki/Tetrahydrofuran>.

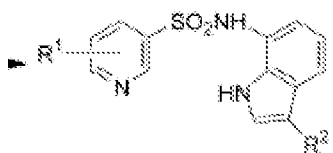
Determination of the scope and contents of the prior art.

Haneda et al. discloses the synthesis of 3-Cyano-N-(3-cyano-4-methyl-1H-indole-7-yl)benzenesulfonamide by dissolving 7-amino-3cyano-4-methyl-1H-indole in tetrahydrofuran, and then pyridine and 3-Cyanobenzenesulfonyl Chloride were added thereto (page 11, Example 1). Haneda et al. also discloses the production of 7-Amino-3cyano-4-methyl-1H-indole (page 8, Production Example 12) through the reduction of 3-Cyano-4-methyl-7-nitro-1H-indole (page 7, Production Example 6), which was made by dissolving 3-Formyl-4-methyl-7-nitro-1H-indole (i.e. which was made by adding phosphorus oxychloride in DMF to 4-Methyl-7-nitro-1H-indole in DMF, page 6, Production Example 5) in DMF and adding hydroxylamine hydrochloride and pyridine.

Owa et al. discloses the reaction of compound 6 (Scheme 1, page 2098) with



in pyridine and EtOAc to produce



Crassier et al. discloses (1) an indole ester of the formula II is formylated and that the formylation is particularly preferably carried out in DMF in the presence of POCl₃ (page 6, line 10), (2) the formyl ester of the formula III formed from (1) is reacted with hydroxylamine to give an oxime derivative of the formula IV and (3) the oxime of the formula IV is converted into a cyanoindole ester of the formula V (page 2, line 25 through page 3, line 25). Crassier et al. also discloses that in a particular embodiment of the process, steps (1) to (3) are carried out in situ, i.e. in a one-pot process (page 7, line 5) and that the one-pot process gives better yields compared with the stepwise synthesis.

<http://en.wikipedia.org/wiki/Tetrahydrofuran> discloses that THF tends to form peroxides on storage in air (i.e. under "Precautions").

Ascertaining the differences between the prior art and the claims at issue.

Haneda et al. discloses the synthesis of 3-Cyano-N-(3-cyano-4-methyl-1H-indole-7-yl)benzenesulfonamide in a different solvent (i.e. tetrahydrofuran) than the instant claims (i.e. a mixed solvent of water and C1-6alkyl acetate) although the base, reactant and product are exactly the same as the instant claims. Haneda et al. also discloses that the synthesis steps to make 3-Cyano-4-methyl-7-nitro-1H-indole are not carried out in situ although all the solvents, reagents, reactants and products are identical to those of the instant claims.

Owa et al. discloses the synthesis of the N-(7-Indolyl)-3-pyridinesulfonamide derivatives in a slightly different solvent (i.e. EtOAc) than the instant claims although the base, reactants and products are exactly the same.

Crassier et al. discloses the synthesis to make compounds of formula V (page 3, line 25) as a one-pot process and with the same solvents and reagents as the instant claims, however, the indole derivatives are slightly different structurally than those of the instant claims.

Resolving the level of ordinary skill in the pertinent art – Prima Facie Case of Obviousness.

Art Unit: 1626

It would have been obvious to one of ordinary skill in the art at the time of the invention to carry out the processes of the instant claims in view of the aforementioned references. It is common practice for a person skilled in the art to carry out a synthesis in different solvent conditions in an attempt to optimize a synthesis. Further, the courts have stated that changes in process conditions of an old process does not impart patentability in the absence of unexpected results. In re Boesch, 205 USPQ 215 (1980). In re Aller et al. (CCPA 1955) 220 F2d 454. In re Dunn, 146 USPQ 479 (i.e. use of a conventional solvent in an other wise known process is not a patentable modification). Also, it was known in the art at the time of the invention that THF, which is an ether, tends to form peroxides, so carrying out the reaction in different solvents would have been obvious.

In regards to the one-pot synthesis of 3-Cyano-4-methyl-7-nitro-1H-indole, it would have been obvious to attempt to carry out this synthesis in a one-pot synthesis in view of Crassier et al.

One of ordinary skill would have reasonable expectation of success in practicing the instantly claimed processes. One would be motivated to carry out the instant processes in an attempt to find optimal conditions for carrying out a known process. Therefore, the instant claims are *prima facie* obvious.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Art Unit: 1626

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KRISTIN BIANCHI whose telephone number is (571)270-5232. The examiner can normally be reached on Mon-Fri 7am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/
Primary Examiner, Art Unit 1626

Kristin Bianchi
Examiner
Art Unit 1626
